18 November 2008

This supplement has been prepared to present scientific and technical news items that may be of more interest to technical personnel at RDT&E activities and the labs, or the medics rather than the broader readership of the basic CB Daily. Due to the nature of the material, the articles, if available online, are usually only available through subscription services thus making specific links generally unavailable. Thus, usually only the bibliographic citation is available for use by an activity's technical library.

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Chem-Bio News– Pandemic Influenza Supplement # 36

1. SINDBIS VIRUS VECTORS ELICIT HEMAGGLUTININ-SPECIFIC HUMORAL AND CELLULAR IMMUNE RESPONSES AND OFFER A DOSE-SPARING STRATEGY FOR VACCINATION: *"This demonstrated the dose-sparing capacity of the SIN vector system and its ability to stimulate long-term memory responses, properties that are highly desirable in any vaccine formulation."*

2. 1918 SPANISH FLU RECORDS COULD HOLD THE KEY TO SOLVING FUTURE PANDEMICS: *"Ninety years after Australian scientists began their race to stop the spread of Spanish flu in Australia, University of Melbourne researchers are hoping records from the 1918 epidemic may hold the key to preventing future deadly pandemic outbreaks."*

3. AN AVIAN LIVE ATTENUATED MASTER BACKBONE FOR POTENTIAL USE IN EPIDEMIC AND PANDEMIC INFLUENZA VACCINES: "*The results presented in this report suggest that the internal genes of a genetically modified AIV confer similar protection in a mouse model and thus could be used as a master donor strain for the generation of live attenuated vaccines for epidemic and pandemic influenza."*

4. AN INHIBITORY ACTIVITY IN HUMAN CELLS RESTRICTS THE FUNCTION OF AN AVIAN-LIKE INFLUENZA VIRUS POLYMERASE: *"Understanding the molecular basis of this species-specific restriction should provide strategies to prevent and treat avian influenza outbreaks in humans."*

5. INFLUENZA VIRUSES AND THE NF-KAPPAB SIGNALING PATHWAY - TOWARDS A NOVEL CONCEPT OF ANTIVIRAL THERAPY: *"Furthermore, the unexpected viral dependency on a cellular signaling factor may pave the path for novel antiviral approaches targeting essential cellular components rather than viral factors."*

6. TOWARD A BROADLY PROTECTIVE INFLUENZA VACCINE: *"These peptides could be used to add a CD8+ T cell component to current antibody-focused vaccine strategies with a view to reducing the impact of infection with novel influenza A viruses."*

CB Daily Report

Chem-Bio News

SINDBIS VIRUS VECTORS ELICIT HEMAGGLUTININ-SPECIFIC HUMORAL AND CELLULAR IMMUNE RESPONSES AND OFFER A DOSE-SPARING STRATEGY FOR VACCINATION
Gene Therapy Weekly
November 13, 2008

"We report here on the use of a Sindbis virus-based DNA-launch RNA replicon vector (pSIN-HA) that expresses influenza hemagglutinin (HA) as an immunogen. Immunization of mice with pSIN-HA generated anti-HA antibody and CTL responses and resulted in lower lung viral titers after influenza challenge when compared to controls."

"Importantly, immunization with a low dose of pSIN-HA mediated significantly reduced lung viral titers following challenge at 43 weeks after the final immunization. In contrast, immunization with a non-replicon DNA vector expressing HA failed to mediate reduced lung viral titer at the same dose."

"This demonstrated the dose-sparing capacity of the SIN vector system and its ability to stimulate long-term memory responses, properties that are highly desirable in any vaccine formulation."

The full article can be found at: (A. Miller, et. al., “Sindbis virus vectors elicit hemagglutinin-specific humoral and cellular immune responses and offer a dose-sparing strategy for vaccination”. Vaccine, 2008;26(44):5641-8). Link not available.

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1918 SPANISH FLU RECORDS COULD HOLD THE KEY TO SOLVING FUTURE PANDEMICS
Infection Control Today Magazine
November 10, 2008

“Ninety years after Australian scientists began their race to stop the spread of Spanish flu in Australia, University of Melbourne researchers are hoping records from the 1918 epidemic may hold the key to preventing future deadly pandemic outbreaks.”

“Professorial Fellow John Mathews and colleagues are analyzing the records of 24,000 people collected from 12 locations in the UK during the Spanish flu outbreak including CambridgeUniversity, public boarding schools and elementary schools.

He says gaining a better understanding of how and why the virus spread will help health authorities make decisions about how to tackle future pandemics.

"In the 1918/19 pandemic, mortality was greatest among previously healthy young adults, when normally you would expect that elderly people would be the most likely to die,'' Mathews says "We don't really understand why children and older adults were at lesser risk.

"One explanation may be that children were protected by innate immunity while older people may have been exposed to a similar virus in the decades before 1890 which gave them partial but long-lasting protection. Those born after 1890 were young adults in 1918. They did not have the innate immunity of children and as they weren't exposed to the pre-1890 virus they had little or no immunity against the 1918 virus. We can't prove it but it is a plausible explanation."

The full article can be found at: http://www.infectioncontroltoday.com/hotnews/key-to-future-pandemics.html

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AN AVIAN LIVE ATTENUATED MASTER BACKBONE FOR POTENTIAL USE IN EPIDEMIC AND PANDEMIC INFLUENZA VACCINES
Biotech Week
November 19, 2008

“The present study focused on the protective effects of a genetically modified AIV as a source for the preparation of vaccines for epidemic and pandemic influenza."

"It has previously been demonstrated that a live attenuated AIV based on the internal backbone of influenza A/Guinea fowl/Hong Kong/WF10/99 (H9N2), called WF10att, is effective at protecting poultry species against low-and high-pathogenicity influenza strains. More importantly, this live attenuated virus provided effective protection when administered in ovo. In order to characterize the WF10att backbone further for use in epidemic and pandemic influenza vaccines, this study evaluated its protective effects in mice. Intranasal inoculation of modified attenuated viruses in mice provided adequate protective immunity against homologous lethal challenges with both the wild-type influenza A/WSN/33 (H1N1) and A/Vietnam/1203/04 (H5N1) viruses. Adequate heterotypic immunity was also observed in mice vaccinated with modified attenuated viruses carrying H7N2 surface proteins.

"The results presented in this report suggest that the internal genes of a genetically modified AIV confer similar protection in a mouse model and thus could be used as a master donor strain for the generation of live attenuated vaccines for epidemic and pandemic influenza."

The full article can be found at: (D. Hickman, et. al., “An avian live attenuated master backbone for potential use in epidemic and pandemic influenza vaccines”. Journal of General Virology, 2008;89(Pt 11):2682-90). Link not available.

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AN INHIBITORY ACTIVITY IN HUMAN CELLS RESTRICTS THE FUNCTION OF AN AVIAN-LIKE INFLUENZA VIRUS POLYMERASE

Health & Medicine Week
November 17, 2008

"Transmission of avian influenza virus into human populations has the potential to cause pandemic outbreaks. A major determinant of species tropism is the identity of amino acid 627 in the PB2 subunit of the heterotrimeric influenza polymerase; glutamic acid predominates in avian PB2, whereas lysine occupies this position in human isolates."

"We show that a dominant inhibitory activity in human cells potently and selectively restricts the function of polymerases containing an avian-like PB2 with glutamic acid at residue 627. Restricted polymerases fail to assemble into ribonucleoprotein complexes, resulting in decreased genome transcription, replication, and virus production without any significant effect on relative viral infectivity."

"Understanding the molecular basis of this species-specific restriction should provide strategies to prevent and treat avian influenza outbreaks in humans."

The full article can be found at: (A. Mehle, et. al., “An inhibitory activity in human cells restricts the function of an avian-like influenza virus polymerase”. Cell Host & Microbe, 2008;4(2):111-122). Link not available.

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INFLUENZA VIRUSES AND THE NF-KAPPAB SIGNALING PATHWAY - TOWARDS A NOVEL CONCEPT OF ANTIVIRAL THERAPY

Pharma Investments, Ventures & Law Weekly
November 16, 2008

One of the hallmark signaling factors activated by viral pathogens is the transcription factor NF-kappaB. Activation of NF-kappaB leads to the up-regulation of a variety of antiviral genes. Thus, the factor is commonly regarded as a major regulator of the innate immune defense to infection. However, several recent studies indicate that influenza viruses have acquired the capability to reprogram this antiviral activity and to exploit the factor for efficient replication. These data provide novel insights into the pathophysiological function of NF-kappaB in the special environment of a virus-infected cell."

"Furthermore, the unexpected viral dependency on a cellular signaling factor may pave the path for novel antiviral approaches targeting essential cellular components rather than viral factors."

The full article can be found at: (S. Ludwig, et. al., “Influenza viruses and the NF-kappaB signaling pathway - towards a novel concept of antiviral therapy”. Biological Chemistry, 2008;389(10):1307-12). Link not available.

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TOWARD A BROADLY PROTECTIVE INFLUENZA VACCINE
Pharma Investments, Ventures & Law Weekly
November 16, 2008

“The current inactivated influenza virus vaccines induce antibodies that protect against closely related virus strains. They do not, however, protect against antibody-escape variants of seasonal influenza A viruses or new pandemic influenza A viruses emerging from non-human reservoirs."

"Might boosting influenza A virus-specific CD8+ T cell memory diminish the danger posed by these variant viruses? Pre-existing CD8+ T cell-mediated immunity directed at peptides from conserved internal proteins of the influenza A virus does not prevent infection, but it can promote early virus clearance and decrease morbidity in mice. In this issue of the JCI, Lee et al. show that people who have not been exposed to avian influenza A (H5N1) viruses have cross-reactive CD8+ T cell memory to a wide range of H5N1 peptides.”

"These peptides could be used to add a CD8+ T cell component to current antibody-focused vaccine strategies with a view to reducing the impact of infection with novel influenza A viruses."

The full article can be found at: (P.C. Doherty, et. al., “Toward a broadly protective influenza vaccine”. Journal of Clinical Investigation, 2008;118(10):3273-5). Link not available.

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